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EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,133	AU-YOUNG ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) *30,32-34 and 37-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-29,31,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Response filed 10/3/03 has been entered. Applicant has cancelled claims 1-20 and added new claims 21-40.

Applicant's election with traverse of Group 23 (claims3-4, 9-14), which includes new claims 23-29 and 31 (replacing original claims 3-4 and 9-14), drawn to polynucleotides encoding a polypeptide comprising the amino acid set forth in SEQ ID NO:1-13 and SEQ ID NO:16-16, vector, host cell, and method of producing a polypeptide of SEQ ID NO:1-13 and SEQ ID NO:16-18, on 10/3/03 is acknowledged. Further Applicants elected, with traverse, to prosecute claims related to the polynucleotide encoding the polypeptide sequence of SEQ ID NO:7, which sequence include SEQ ID NO:25, and which sequences read on new claims 21-22 and 35-36 (replacing original claims 1, 2 and 15). The traversal is on the ground(s) that the claims should be examined according to the principles of the PCT unity of invention guidelines. Applicant request claims 21-29, 31 and 35-36 be examined in a single application. Applicant request rejoinder of method claims upon allowance of product claim in light of *In re Ochiai, In re Brouwer* and 35 USC 103 (b). Applicant's arguments have been considered and found persuasive. Upon allowance of the product claims, the process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

A search of Groups 1-128 would not be co-extensive particularly with regard to the literature search. An examination of the materially different, patentably distinct

inventions in a single application would constitute a serious undue burden on the examiner. Claims 30, 32-34 and 37-40 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The requirement is still deemed proper and is therefore made FINAL.

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

3. **Objections**

The disclosure is objected to because of the following informalities:

Applicants are required to use the heading "Brief Description of the Drawings" to describe the drawings. See MPEP 608.01(f). On page 21, Applicant has written "BRIEF DESCRIPTION OF THE FIGURES AND TABLES"

Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-29, 31 and 35-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21 and 31 are indefinite because it is not clear when a nucleic acid molecule or polypeptide is considered naturally occurring as compared to when it is not naturally occurring so as to allow the metes and bounds of the claim to be determined. If one makes a nucleic acid molecule or polypeptide having at least 90% sequence identity to SEQ ID NO:25 or SEQ ID NO:7, respectively, in the laboratory, by randomly mutating, say one base, of the nucleic acid molecule disclosed in SEQ ID NO:2, would said mutated nucleic acid molecule be considered "naturally occurring" or not "naturally occurring". At this moment in time this determination is impossible to make. Not until every possible sequence and mutation in every living cell has been determined, to serve as a comparison, can one even begin to formulate an opinion as to wheatear the nucleic acid molecule is "naturally occurring". If the mutation created in the laboratory, which was initially classified as not naturally occurring, is found in a living cell, does the nucleic acid molecule then become naturally occurring? Therefore by merely looking at a nucleic acid molecule it can be determined is a sequence is naturally nucleic acid molecule as compared to not naturally occurring. What specific critical feature of the invention allows the nucleic acid molecule to be classified as naturally occurring as compared to not naturally occurring? Further any recombinant nucleic acid introduced into a host cell and that replicates in said host cell could be considered naturally occurring.

Claim 21 is indefinite because it is not clear what constitutes a biologically active fragment since no activity is disclosed for the claimed polypeptide.

Claim 31 is indefinite because it is not clear what constitutes a RNA equivalent of a)-c).

Claims 22-29 and 35-36 are rejected for depending upon an indefinite base (or intermediate) claim and fail to resolve the issues raised above.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 22-29, 31 and 35-36 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specifications disclosure of the

properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention. Applicant has asserted utilities for the specifically claimed invention of claims 21-29, 31 and 35-36. The invention is directed to:

i) a) isolated polypeptide comprising the amino acid sequence of SEQ ID NO:7, b) naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:7, c) a biologically active fragment of a polypeptide having the amino acid sequence of SEQ ID NO:7, d) an immunogenic fragment of the polypeptide of SEQ ID NO:7

ii) isolated polynucleotide encoding the polypeptide of i)

iii) a) isolated polynucleotide comprising the polynucleotide sequence of SEQ ID NO:25, b) polynucleotide comprising a naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:25, c)polynucleotides complementary to a) and b), d) RNA equivalent of a)-c).

vii) recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of ii) and cell transformed with said recombinant polynucleotide

viii) method of producing the polypeptide of I)

The claims encompasses nucleic acid molecules encoding variants of the protein disclosed in SEQ ID NO:7, said variants may be completely unrelated, structurally and functionally to the protein encoded by the polynucleotide of SEQ ID NO:25.

The specification discloses the channel protein of SEQ ID NO:7 (MECHP-7) is encoded by the polynucleotide of SEQ ID NO:25. MECHP-7 is shown to have 84% homology to mouse connexin 30.3. The activity/functionality of MECHP-7 and mouse

connexin 30.3 polypeptide is not disclosed. The superfamily of ion channels are highly divergent in their effects, solutes transported and ligand specificity as disclosed in the specification. The outcome of the cellular signaling effect varies depending on the, ion channel, ion transported, activating ligand. There is no disclosure of the specific compounds transported or specific ligands that activate or bind claimed MECHP-7. Based solely on the homology data to other connexin 30.3 and the general classification into the superfamily of ion transporters, the specification discloses the claimed MECHP-7 is believed to be a channel protein. The exact role of MECHP-7 in any disease state or non disease state has not been disclosed. The specification discloses the MECHP can be used to treat or prevent a disorder associated with decreased expression or activity of hundreds of unrelated diseases (pages 33-36). The specification further discloses in treatment of disorders associated with increased MECHP expression or activity, it is desirable to decrease the expression or activity of MECHP. In the treatment of disorders associated with decreased MECHP expression or activity, it is desirable to increase the expression or activity of MECHP. There is no disclosure of the specific disease state involved in MECHP-7 dysfunction, or whether its expression is increased or decreased. Therefore it is not known which disease to treat by altering expression of MECHP-7. It is not known whether increased expression is beneficial or detrimental to the host. It is not known whether increased expression is detrimental to the host. There is no disclosure of the specific activity of claimed MECHP-7 or how to assay for said activity. In light of the specification the skilled artisan can not come to any conclusions as to the function of claimed nucleic acid encoding the MECHP-7or variants thereof.

The specification discloses the claimed invention can be used for diagnosis, treatment or prevention of cell proliferation, immune/inflammatory, transport/secretory, osmoregulatory, muscular, cardiovascular and neurological diseases. There is no nexus between the diseases treated. The utility of claimed protein cannot be implicated solely from homology to the proteins known in the art because the art does not provide teaching stating that all protein disclosed have the same activity, same effects, the same ligands and are involved in the same disease states. In light of the specification and art the skilled artisan can not come to any conclusions as to the function of protein encoded by claimed nucleic acid. There is no disclosure provided within the instant specification on what specific function the protein of SEQ ID NO:7 possesses, or how to specifically assay for such, ligands that bind, promoters that activate; nor are any cell types/tissues disclosed that specifically nor are any disease states disclosed that are directly related to said protein dysfunction.

The specification fails to disclose, what specific disease is associated with claimed MECHP-7 dysfunction or what drugs affect MECHP-7. The claims, specification, nor prior art disclose the ligand that binds claimed ion channel, the activity associated with claimed MECHP-7 or, how the activity is modulated, and how the modulation or activity is determined using specific assay steps. The claimed MECHP-7 may have utility in the future, when it has been further characterized (e.g. its dysfunction or function correlated with a disease state) and its ligand or compound transported characterized and functionality determined. The inclusion in the family of ion channels does not constitute either a specific and substantial asserted utility or a well

established utility for that particular MECHP-7 or protein. This is analogous to all proteins/nucleic acid of ion channels can be used as markers on a gel.

Specification discloses claimed MECHP-7 are useful in screening but the specification does not disclose what claimed MECHP-7specifically regulates and what specific disease, claimed MECHP-7, is a target for. What would be the use of using the claimed MECHP-7on a panel for drug screening? The MECHP-7has no known ligand or known function. How would one use the compounds that interacted with said orphan MECHP-7? It is unpredictable what ligands will bind to orphan MECHP-7 and which compounds are transported. Further the functional effects of ligand binding and compound transport may remain uncertain even after extensive experimentation. What is the utility for a ligand ,in many cases with no known function, that binds to a MECHP-7 of no known function? The ordinary artisan can only speculate on the utility for the ligand and MECHP-7. A utility to orphan MECHP-7 cannot be assigned without knowledge of what disease is associated with claimed MECHP-7 dysfunction or what drugs/ligands effect a specific claimed MECHP-7function. The superfamily of ion transporters are highly divergent in their effects and compound specificity. The utility of claimed MECHP-7 cannot be implicated solely from homology to known ion channels or their protein domains because the art does not provide teaching stating that all members of family of ion channels must have the same effects, the same ligands and be involved in the same disease states, the art discloses evidence to the contrary. Specification has used protein domains/homology are predictive as to the activity of the protein. The utility of claimed receptor cannot be implicated solely from homology to known ion channels or their protein domains because the art does not provide teaching stating that all members

of family of ion channels must have the same effects, the same ligands, transport the same compound and be involved in the same disease states, the art discloses evidence to the contrary (see above)

Bork (Nature Genetics, Vol.18, pages 313-318, 1998) provide a review article disclosing the problems of using homology detection methods to assigning function to related members of a family. Bork discloses: a) "While current homology detection methods can cope with data flow, the identification, verification and annotation of functional features need to be drastically improved", page 313, column 1, Abstract, b) there are two bottle necks that need to be overcome en route to efficient functional predictions from protein sequences, i.e., "First, there is the lack of a widely accepted, robust and continuously updated suite of sequence analysis methods integrated into coherent and efficient prediction system. Second, there is considerable 'noise' in the presentation of experimental information, leading to insufficient or erroneous function assignment in sequence databases", page 313, column 1, third paragraph, c) "In-depth analysis of protein sequences often results in functional predictions not attained in the original studies", page 313, column 2, last paragraph, d) "However, more often than not, it is clear that the cellular role of the protein in question differs from that of the detected homologue(s) and there is currently no automatic means to establish how much functional information can be legitimately transferred by analogy from homologue to the query", page 315, column 2, last paragraph, e) pertaining to predictions of protein function, "Do not simply transfer functional information from the best hit. The best hit is frequently hypothetical or poorly annotated; other hits with similar or even lower scores may be more informative; even the best hit may have a different function", while "many

proteins are multi functional; assignment of a single function, which is still common in genome projects, results in loss of information and outright errors" and "It is typical that the general function of a protein can be identified easily but the prediction of substrate specificity is unwarranted; for example, many permeases of different specificity show approximately the same level of similarity to each other", page 316. Karp (Bioinformatics, Vol 14, No.9, pages 753-754, 1998) has disclosed the problems of using functional prediction based on homology analysis. Karp states, a) "Although we know the accuracy with which sequence homologs can be determined, we know little about the accuracy of the overall process of assigning function by homology, page 753, column 2, second paragraph, b) "We have more faith in the correctness of those sequences whose functions we determined experimentally, rather than through computational means, page 753, column 2, last paragraph, c) "research is required to estimate the error rate of functional annotation by different methods of computational sequence analysis", page 754, column 2, last paragraph. Bork (Current Opinion in Structural Biology, Vol 8, pages 331-332, 1998), discusses the problems with deriving biological knowledge from genomic sequences and states, "structural similarity does not lead to iron-clad functional predictions" page 331, column 2 last paragraph, "Structural similarity does not necessarily mean a common evolutionary origin" page 332, column 1, second paragraph, and "Today, what we predict from sequences is at best fragmentary and qualitative", page 332, column 2, second paragraph. Therefore, references discussed above disclose the unpredictability of assigning a function to a particular protein based on homology, especially one that belongs to the family of sodium/solute symporters which have very different ligand specificity and functions.

It can be argued the claimed MECHP-7are useful as tools as reagents and targets as a molecular target in the diagnosis and treatment of claimed MECHP-7mediated disorders. All members of the ion channels family have a utility in selectively screening of candidate drugs that target ion channels. However, for a utility to be "well-established" it must be specific, substantial. In this case, as all MECHP-7 are in some combination useful in selectively screening of candidate drugs that target ion transporters and in toxicology testing. However, the particulars of screening of candidate drugs, that target claimed MECHP-7, and in toxicology testing are not disclosed in the instant specification. Neither the candidate drugs or toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO:7 and 25. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed protein for screening compounds that are a target for claimed MECHP-7is only useful in the sense that the information that is gained from the assay and is dependent on the effect it has on the protein, and says nothing with regard to each individual member of the MECHP-7family. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicants' individual MECHP-7is affected by a test compound in an assay for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this

consideration, the individually claimed method of using claimed MECHP-7 has no "well-established" use. The artisan is required to perform further experimentation on the claimed MECHP-7itself in order to determine to what "use" any information regarding this protein could be put.

With regard to diagnosis of disease, in order for a polynucleotide or protein to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed MECHP-7and a disease or disorder. The presence of claimed MECHP-7in tissue is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed MECHP-7 and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed MECHP-7 to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed MECHP-7is either present only in, e.g. cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. over expression). Evidence of a differential expression might serve as a basis for use of claimed MECHP-7as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed MECHP-7and any disease or disorder and the lack of any correlation between the claimed VR-L with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of

use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

Further, ion channel family to which the polypeptide encoded by the polynucleotide of SEQ ID NO:25 belongs is a family in which the members have divergent functions based on which tissues the protein is expressed or administered to. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific and utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family. The diversity of the ion channel family has already been described. Without some common biological activity for the family members, a new member would not have a specific or substantial utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. To argue that all the members can be used for drug screening, toxicology testing and diagnosis, is to argue a general, nonspecific utility that would apply to virtually every member of the family, contrary to the evidence. Further, any compound could be considered as a regulator or modulator of tissue in that any compound, if administered in the proper amount, will stimulate or inhibit tissue. For example, salt,

ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of tissue. However, use of these compounds for the modulation of tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use.

Without knowing a biological significance of the claimed MECHP-7, one of ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible "real world" manner based on the diversity of biological activities possessed by the ion channel family. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

The assertion that the claimed invention has utility in drug screening, drug development and disease diagnosis, do not meet the standards for a specific, substantial or well-established utility for reasons set forth above. None of the utilities identified have been demonstrated to be specific to the polypeptide encoded by the nucleic acid of SEQ ID NO:25 . One of ordinary skill in the art must understand how to achieve an

immediate and practical benefit from the claimed species based on the knowledge of the class. However, no practical benefit has been shown for the use of the polypeptide SEQ ID NO:7 or the polynucleotide of SEQ ID NO:25. Applicant has failed with respect to claimed MECHP-7, has not described the family of MECHP-7in enough detail to show, by a preponderance of the evidence, that the polypeptide of SEQ ID NO:7 or the polynucleotide of SEQ ID NO:25 or variants thereof has any substantial use. The record shows that the family of proteins having ion channel domains is diverse, and has such a broad definition, that a "common utility" cannot be defined. Moreover, the evidence of record is inadequate to determine the disease(s), drug(s) or toxicological screen(s) for which the compounds would be useful. In *Brenner,* the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible tumor-inhibiting effects and an adjacent homologue of the compound had proven effective. *Brenner*, 148 USPQ at 690. Here, there is no evidence that the claimed isolated compounds have any utility.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention.

The use of the claimed invention for toxicology testing, drug discovery, and disease diagnosis are not substantial utilities. The question at issue is whether or not the broad general assertion that the claimed MECHP-7 might be used for some diagnostic application in the absence of a disclosure of which diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe

that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

The prior rejection under § 101 followed *Brenner v. Manson*. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. A rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967). Further since the claimed MECHP-7has no utility, methods of its use are also rejected for lack of utility.

6. Claims 20-29, 31, 35-36 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither

the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed MECHP-7, polynucleotide (SEQ ID NO:25) encoding the polypeptide of SEQ ID NO:25, variants thereof. Further experimentation is necessary to attribute a utility to the claimed nucleic acid encoding MECHP-7 polypeptides and variants thereof and methods of use.

The claims fail to disclose how to use the claimed invention for the reasons given above (lack of utility). Further the claims are drawn to an orphan MECHP-7. The claimed nucleic acid encodes an orphan MECHP-7 whose activity, compound transported, activating ligands and functionality have not been disclosed. Neither the claims nor the specification disclose what specific biological activity is associated with the claimed MECHP-7. There is no disclosure of the specific compounds that are transported, proteins activated in the signal transduction pathway or what ligand is capable of binding to the polypeptide encoded by the claimed polynucleotide, so as to disclose a specific function for the claimed polynucleotide. Therefore nucleic acid encoding unrelated and inactive proteins are encompassed by the claims. The specification does not disclose how to produce active variants or how to use inactive ones. Substitutions/mutation that result in active variants are not disclosed. Substitutions/mutations that are detrimental to MECHP-7 variant activity are not disclosed. There is no disclosure of how to assay variants since compound transported, natural ligand and function of the claimed invention is unknown.

The complex nature of ion transporters and the unpredictability of assigning a function to MECHP-7 with no known ligand, compound transported, or function is

described in the rejection under 35 USC § 101 and 35 USC § 112, 1st paragraph, also see the teachings of, Karp and Bork, disclosed above.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

The specification does not disclose the critical feature of the invention which is required for activity. For example which fragments are biologically active, and what is said biological activity of MECHP-7. Further, many of the polypeptides of MECHP-7 may be inactive or unrelated to the nucleic acid encoding the polypeptide of SEQ ID NO:7. Further many of the nucleic acids encoding variants 90% identical to MECHP-7 encompassed by the claims may be inactive or unrelated to the nucleic acid of SEQ ID NO:1 encoding the polypeptide of SEQ ID NO:7. The specification does not disclose how to produce active variants. The specification does not disclose a utility for or how to use said inactive or unrelated polypeptides encoded by claimed nucleic acid molecule. The claimed nucleic acid encodes an MECHP-7 whose activity, compound transported, activating ligands, functionality have not been disclosed. Neither the claims nor the specification disclose what specific biological activity is associated with the claimed MECHP-7. There is no disclosure of how to assay variants of MECHP-7 identified by any procedure, since the ligand, compound transported and function of the claimed invention is unknown.

Furthermore, the specification does not reasonably provide enablement for the scope of use of nucleic acid encoding polypeptides comprising variants 90% identical to the

polypeptide of SEQ ID NO:7, or comprising nucleic acid variants 90% identical to the nucleic acid of SEQ ID NO:25 or encoding variants of MECHP-7 polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification discloses a polynucleotide which encodes MECHP-7. The specification does not teach how to make functional claimed MECHP-7 r variants or to use inactive variants. The prior art teaches that amino acid substitutions produce unpredictable results in a structurally related protein. Furthermore, neither the specification nor the prior art provide any guidance as to which amino acids could be altered, nor does the specification provide any guidance as to how the skilled artisan could use inactive claimed MECHP-7 variants. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation that claimed MECHP-7 variants could be used for any purpose. Further the nucleic acids that comprise variants of SEQ ID NO:25 or encode variants of the polypeptide of SEQ ID NO:7 may not specifically hybridize to the polynucleotide of SEQ ID NO:25 or to the polynucleotide that encodes the polypeptide of SEQ ID NO:7. Applicant has not disclosed how to use said nucleic acids that do not specifically hybridize the polynucleotide of SEQ ID NO:25 or to the polynucleotide that encodes the polypeptide of SEQ ID NO:7. Further the specification does not disclose how to use nucleic acids that comprise variants of SEQ ID NO:25 or encode fragments or variants of the polypeptide of SEQ ID NO:7 without functional activity.

Therefore, pertaining to claimed variants, due to the large quantity of experimentation necessary to identify the nucleic acids encoding polypeptides with the

structural and functional features of instant MECHP-7 (the critical feature of the invention is not disclosed, i.e. structure and function relationship), the lack of direction/guidance presented in the specification regarding the identification, purification, isolation, characterization and assaying (no specific assay disclosed which measures claimed MECHP-7 activity) of claimed invention, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:7 and 25 are also encompassed by the claim), construction of active variants (no disclosure of which amino acids can be mutated and still provide active protein) and the breadth of the claim which fail to recite structural (except for the nucleic acid of SEQ ID NO:25, encoding the polypeptide of SEQ ID NO:7) and functional limitations containing critical feature of the invention, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope. For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. A review of *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed invention. As is evidence in the discussions *supra*, each of these factors has been carefully considered in the instant grounds of rejection, and it is maintained that undue experimentation would be required by the skilled artisan to

use the instant invention. Further since the claimed TMP has no utility, vector comprising the claimed nucleic acid, cell comprising said vector, composition comprising claimed nucleic acid and method of producing polypeptide encoded by claimed nucleic also rejected under 35 USC § 112, 1st paragraph.

Claim Rejection 35 USC § 112, 1st paragraph (Written Description)

7. Claims 21, 23, 26-29, 31 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21, 23, 26-29, 31 and 35 are directed to:

i) a) naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:7, b) a biologically active fragment of a polypeptide having the amino acid sequence of SEQ ID NO:7, c) an immunogenic fragment of the polypeptide of SEQ ID NO:7

ii) isolated polynucleotide encoding the polypeptide of i)

iii) a) isolated polynucleotide comprising a naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:25, b) polynucleotides complementary to a) and b), c) RNA equivalent of a)-b).

vii) recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of ii) and cell transformed with said recombinant polynucleotide

viii) method of producing the polypeptide of i)

The claims encompasses nucleic acid molecules encoding variants of the protein disclosed in SEQ ID NO:7, said variants may be completely unrelated, structurally and functionally to the protein encoded by SEQ ID NO:25 .

The common function of the nucleic acid (SEQ ID NO:25) encoding the polypeptide (SEQ ID NO:7), which is based upon a common property or critical technical feature of the genus claimed is not disclosed. The claims, as written, encompass nucleic acid encoding polypeptides which vary substantially in length and also in amino acid composition. The instant disclosure of a polynucleotide of SEQ ID NO:25 encoding the polypeptide of SEQ ID NO:25 does not adequately describe the scope of the use of the claimed genus, which encompasses a substantial variety of subgenera including polynucleotides, proteins, variants of said polynucleotides and proteins, allelic variants, chimeric constructs, fusion constructs, variants and polynucleotides, which may encode polypeptides completely, unrelated functionally/structurally to the polypeptide of SEQ ID NO:7. A description of a genus of polypeptides/polynucleotides may be achieved by means of a recitation of a representative number of polypeptides/polynucleotides, defined by amino acid/nucleic acid sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Instant specification fails to provide sufficient descriptive information, such as definitive structural and functional features of the claimed genus of polypeptides/polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. For example, what regions and fragments of the claimed

invention contain a definitive structural feature required for protein function? The specification proposes to discover other members of the genus by using screening assays and techniques involving probes, primers, hybridization. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and proteins encompassed. No identifying characteristic or property of the instant polypeptides/polynucleotide is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific polypeptide and nucleotide sequences and the inability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe, enable and use the genus as broadly claimed. The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. It is acknowledged that the skill of the artisan in the molecular biology art is high. However, in the current instance, **there is no clear evidence of activity possessed by the**

claimed genus of nucleic acid molecules encoding variant MECHP-7 polypeptides, the critical special technical feature of the polypeptides or how the critical special technical feature encompassed by the genus claimed relates to function. Because of the lack of guidance in the prior art and current application, one skilled in the art could not predict if the variants MECHP-7 have the same activity as the protein disclosed in SEQ ID NO:7, since no activity is disclosed, or if they contain the domain(s) of SEQ ID NO:7, containing the critical special technical feature of the claimed MECHP-7 , since no critical special technical feature is disclosed.

Pertaining to variants to the nucleic acid/protein 90% identical to SEQ ID NO:25/SEQ ID NO:7 the specification does not disclose the critical feature which must be contained in said nucleic acids/proteins which is required for activity. The skilled artisan cannot envision the detailed chemical structure of the encompassed compounds and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is required. See *Fibers v. Revel*, 25 USPQ d. 1601 at 1606 (CAFC 1993) and *Amen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". Therefore the specification fails to disclose the activity of the claimed genus of polypeptides/polynucleotides, the critical special technical feature of the polypeptides/polynucleotides or how the critical special technical feature encompassed by the fragments and variants of claimed MECHP-7 relates to function. The claims encompass nucleic acids encoding proteins which are structurally and functionally unrelated to the protein/nucleic acid disclosed in SEQ ID NO:7 and 25, respectively. Therefore instant specification fails to provide sufficient descriptive information, such as

definitive structural/ functional features of the claimed genus of nucleic acids/polypeptides . There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no disclosure of the specific activity of claimed MECHP-7 and how it is specifically assayed. The specification nor claims disclose the specific activity of the MECHP-7 of instant invention nor a description of the conserved regions which are critical to the structure and function of the genus claimed.

There is no disclosure of the compound transported by the claimed genus nucleic acids encoding a MECHP-7 or the nature of the signal or specific signal transduction pathway. The claimed nucleic acid encodes an orphan MECHP-7 whose activity, associated function and activating ligands have not been disclosed. The neither specification nor prior art provide a specific assay for the genus claimed. Nucleic acids/proteins comprising variants 90% identical to claimed MECHP-7 may be completely unrelated to the protein encoded by the nucleic acid of SEQ ID NO:25 The complexity of assigning a function and membership into a the genus of proteins is highlighted by Bork and Karp (discussed above), who disclose assigning function by homology is unpredictable by using the complete sequence of an protein, let alone using variants which may not have any domains related to a particular function. Neither the claims nor the specification disclose what specific biological activity is associated with the claimed MECHP-7 or the special technical feature encompassed by specific domains associated with a specific activity of the claimed genus. The superfamily of ion transporters are specialized proteins designed for chemical recognition of ligands, transport of specific compounds, and subsequent transduction of information encoded in

those ligands/compounds to the machinery of the cell. Ion transporters interact with many diverse compounds having diverse effects. The important features which would help to define the MECHP-7 activity and define the genus claimed have not been disclosed in the specification nor prior art. 'Further the activity transduced is not disclosed or how it relates structure to function.

The claims encompass nucleic acids encoding proteins which are structurally and functionally unrelated to the protein of SEQ ID NO:7. Therefore instant specification fails to provide sufficient descriptive information, such as definitive structural/ functional features of the claimed genus of polypeptides/polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The neither specification nor claims disclose the specific activity of the "orphan MECHP-7 " of instant invention, how it is assayed, nor a description of the conserved regions which are critical to the structure and function of the genus claimed. Further vector comprising the claimed nucleic acid, cell comprising said vector, composition comprising claimed nucleic acid and method of using claimed MECHP-7 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

8. No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 703-308-9435. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Michael D. Pak
MICHAEL PAK
PRIMARY EXAMINER

Nirmal S. Basi
Art Unit 1646
12/01/2003